

Osteoporosis

Osteoporosis

- The bones in our skeleton are made of a thick outer shell and a strong inner mesh filled with collagen (protein), calcium salts and other minerals.
- The inside looks like honeycomb, with blood vessels and bone marrow in the spaces between bone.



- Normal bone on left
- Osteoporotic bone on right

Osteoporosis – Definition

- Literally translates as “porous bones”
- Osteoporosis occurs when the holes between bone become bigger, making it fragile and liable to break easily



A progressive systematic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture

Osteoporosis – Primary Causes

- Osteoporosis results from an unhealthy imbalance between two normal activities of bone: bone resorption and bone formation.
- These activities rely on two major types of cells: osteoclasts for bone resorption and osteoblasts for bone formation. The combined processes of bone resorption and bone formation allow the healthy skeleton to be maintained continually by the removal of old bone and its replacement with new bone.
- These combined processes are referred to as bone remodeling or bone turnover. During the first 20–25 years of life, these processes are balanced.

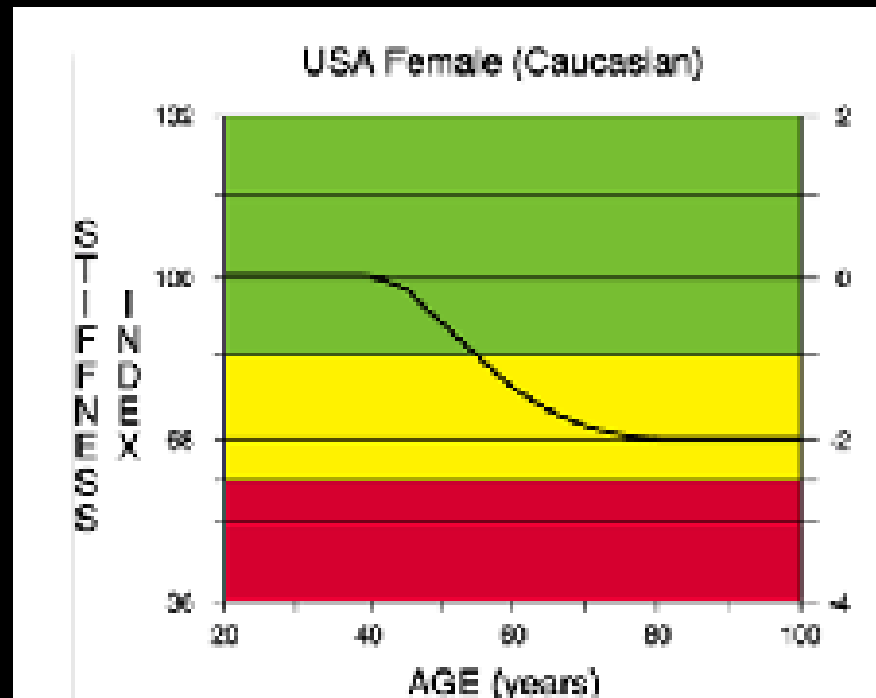
Osteoporosis – Primary Causes

- Following a period of balanced bone resorption and bone formation, the destruction of bone begins to exceed the formation of bone; this imbalance leads to a net loss of bone, and the beginnings of osteoporosis.
- The risk of fracture increases from 1.5 to 3-fold for every 10% decrease in bone mass.
- Bone mineral density (BMD), a measure of bone mass divided by bone area, increases with age until peak bone density is achieved. Bone mineral density is correlated highly with bone strength and is therefore used to quantitatively screen and diagnose patients.

Osteoporosis – Density

- Normal bone density is within 1 SD of the young adult mean
- Osteopenic bone density is between 1 and 2.5 SD below the young adult mean (T-score between 1 and 2.5)
- Osteoporotic bone density is > 2.5 SD below the young adult mean (T-score greater than 2.5)
- Those who fall at the lower end of the young normal range (a T-score of > 1 SD below the mean) have low bone density and are considered to be at increased risk of osteoporosis

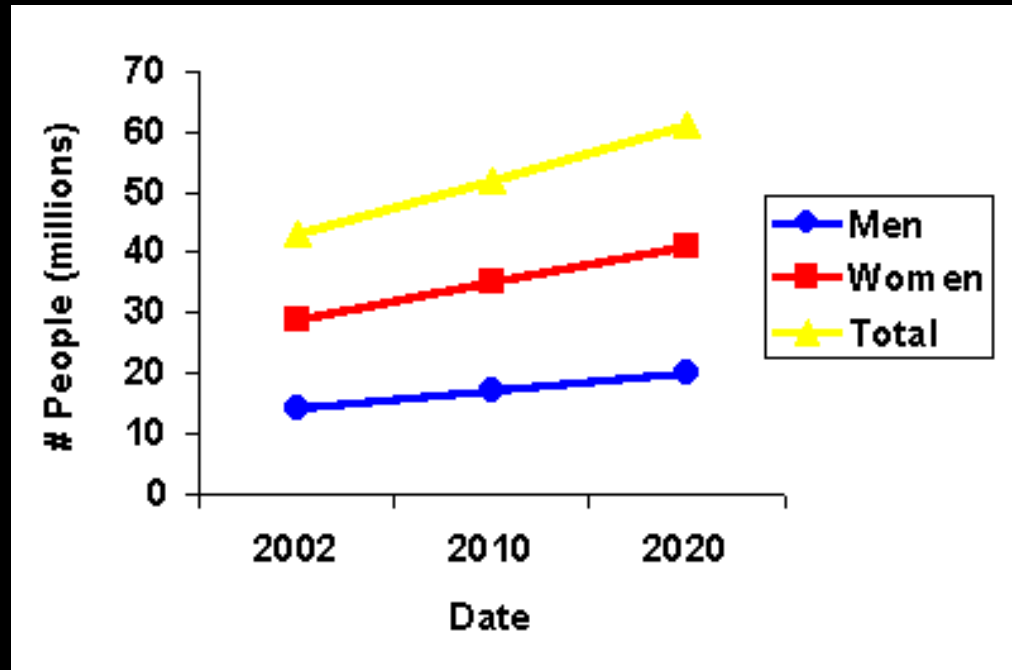
- Degree of bone loss is defined by comparison with young adult mean bone density:



- A Z-score compares your BMD result to others of your same sex, age, and weight.

Osteoporosis – Prevalence

- In the USA, the estimated prevalence of osteopenia is 15 million in women and 3 million in men.
- The estimated prevalence of osteoporosis is 8 million in women and 2 million in men.
- Although, osteoporosis affects >10 million individuals in the United States, only 10 to 20% are diagnosed and treated

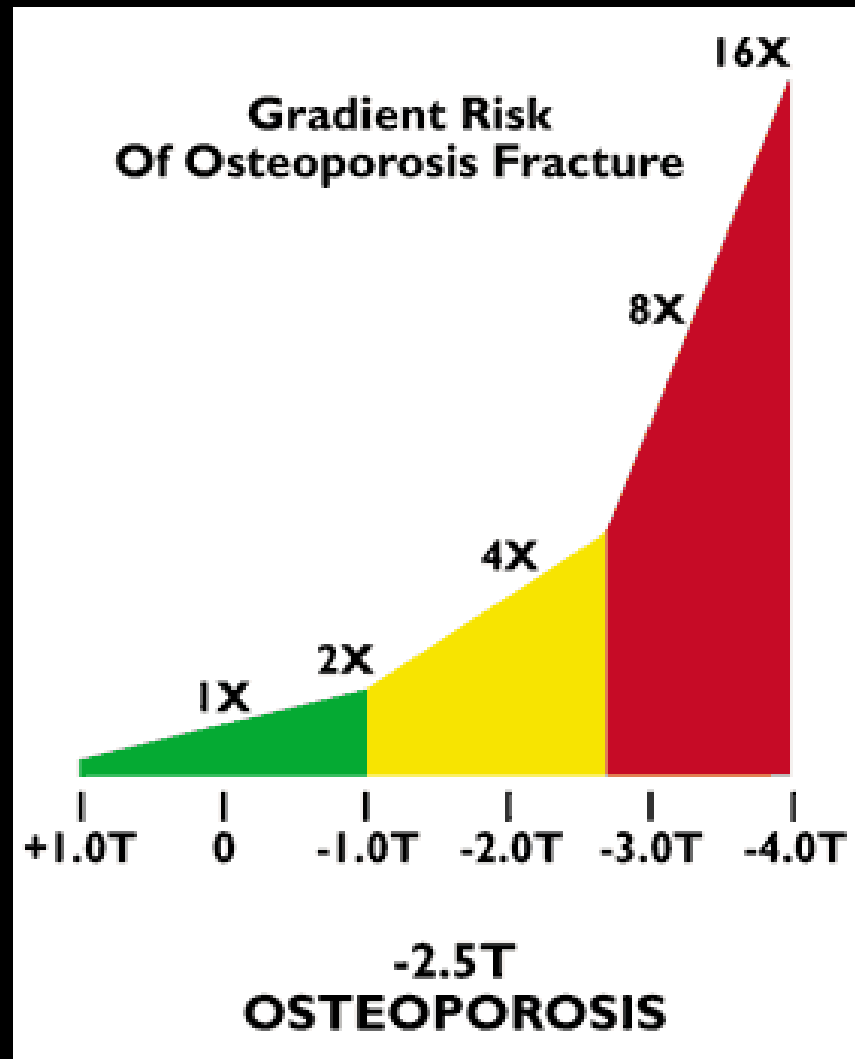


Estimated global prevalence

- Osteopenia and osteoporosis are major public health problems, resulting in substantial morbidity and estimated health costs of >\$14 billion annually.

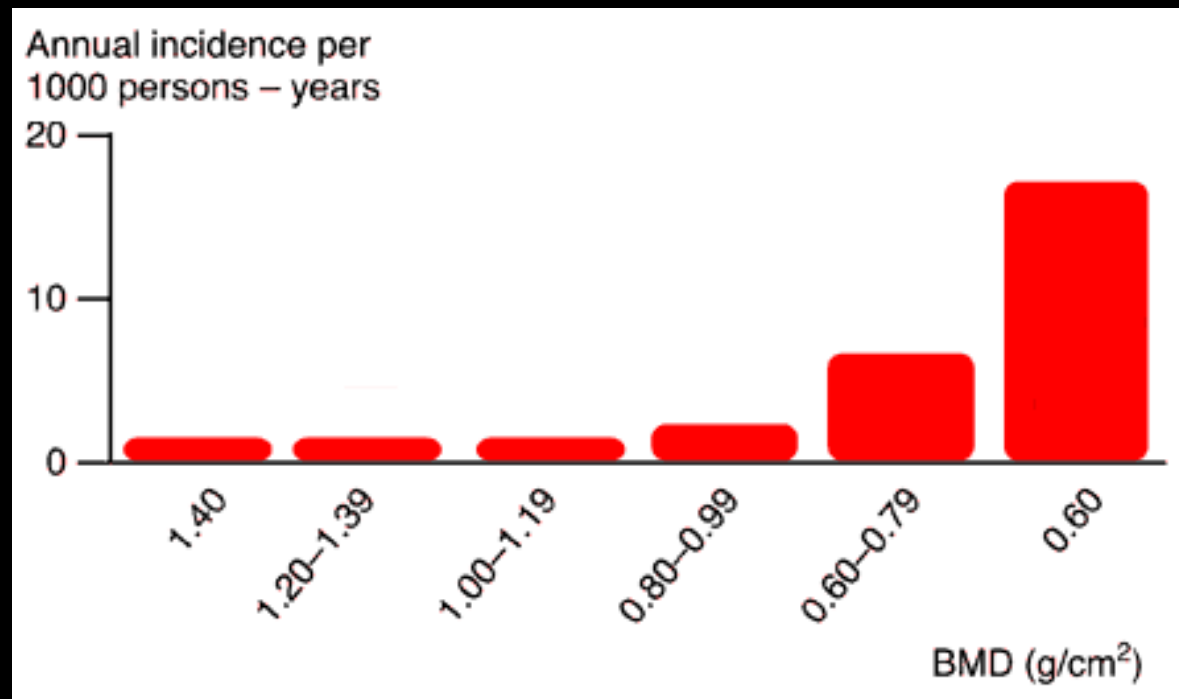
Increased risk of fracture

- Osteoporosis has been termed a silent disease because, until a fracture occurs, symptoms are absent.
- Chief clinical manifestations are vertebral and hip fractures
- Rate of fracture increases exponentially with increasing magnitude of T-scores



Increased risk of fracture

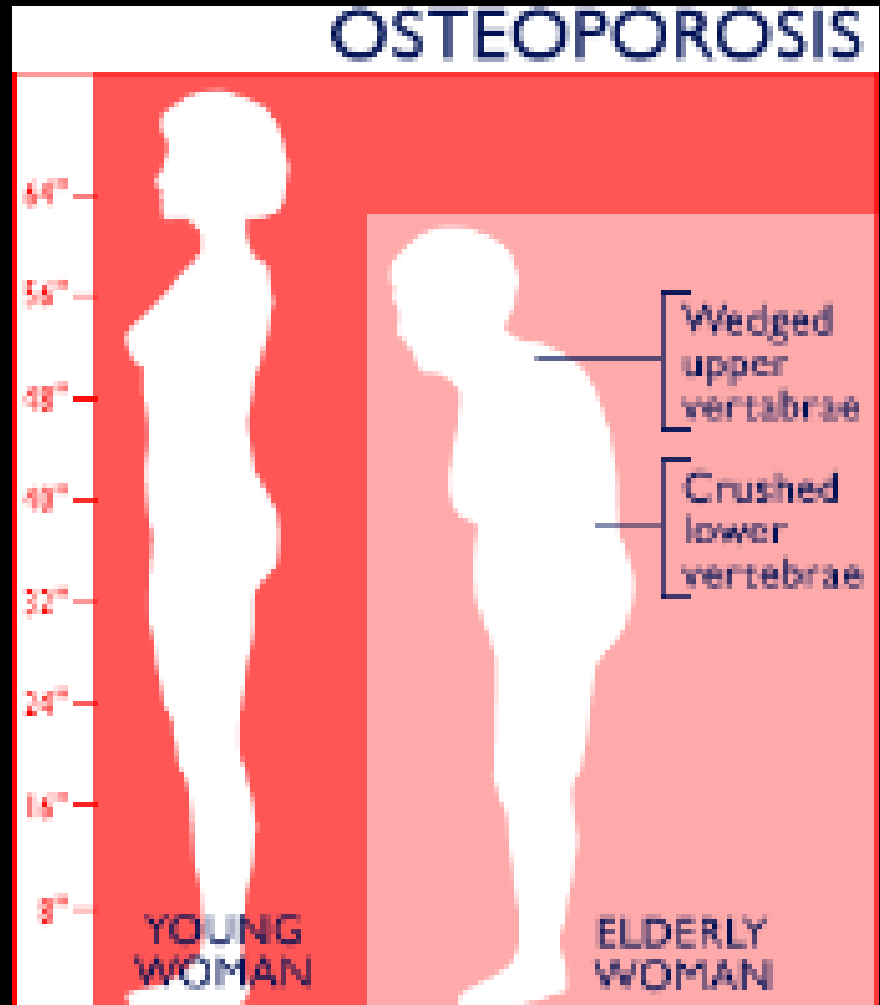
- About 300,000 hip fractures occur each year in the United States
- Hip fractures are associated with a high incidence of deep vein thrombosis and pulmonary embolism (20 to 50%) and a mortality rate between 5 and 20% during the few months after surgery.



Increase in risk of hip fractures with decreased bone density

Increased risk of fracture

- About 500,000 vertebral crush fractures per year in the United States
- Vertebral fractures rarely require hospitalization but are associated with long-term morbidity and a slight increase in mortality. Multiple fractures lead to height loss (often of several inches), kyphosis, and secondary pain and discomfort related to altered biomechanics of the back.



Pathogenesis

- Diminished bone mass can result from:
 - failure to reach an optimal peak bone mass in early adulthood
 - increased bone resorption
 - decreased bone formation after peak bone mass has been achieved
- All three of these factors probably play a role in most elderly persons. Low bone mass, rapid bone loss, and increased fracture risk correlate with high rates of bone turnover (ie, resorption and formation).
- In osteoporosis, the rate of formation is inadequate to offset the rate of resorption and maintain the structural integrity of the skeleton

Aging vs. Osteoporosis

- Bone resorption rates appear to be maintained or even to increase with age
- Bone formation rates tend to decrease.
- Loss of template due to complete resorption of trabecular elements or to endosteal removal of cortical bone produces irreversible bone loss.
- Age-related microdamage and death of osteocytes may also increase skeletal fragility
- **HOWEVER, Osteoporosis is NOT an inevitable consequence of aging;** many persons maintain good bone mass and structural integrity into their 80s and 90s.

Risk Factors

Risk factors that cannot be modified include:

- Caucasian race
- Advanced age
- Female sex
- Premature menopause (<45 years)
- Prolonged time (>1 year) without a menstrual period

Conditions associated with osteoporosis:

- Anorexia nervosa
- Malabsorption syndromes
- Excessive secretion of parathyroid hormone
- Excessive secretion of thyroid hormone
- Post-transplantation
- Chronic renal disease

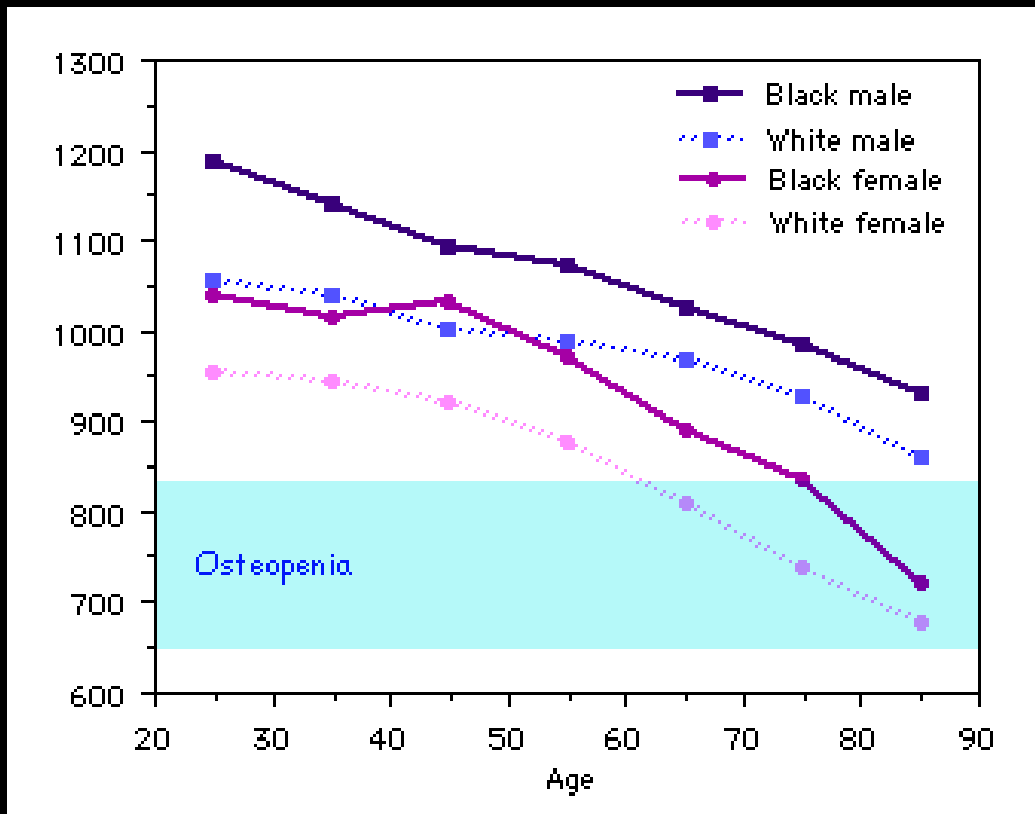
- Chronic liver disease
- Excessive secretion of cortisol (Cushing's syndrome)
- Radiographic evidence of osteopenia or vertebral deformity
- Previous fracture not caused by a major accident
- Cancer
- Significant loss of height or an abnormal bend in the upper spine (thoracic kyphosis)

Risk factors that have the potential to be modified include:

- Cigarette smoking
- Excessive alcohol intake
- Inactivity
- Low body weight
- Poor general health
- Prolonged immobilization

Risk Factors – Gender and Race

	Age 25	Age 50	Age 65	Age 80
Normal	84%	66%	40%	10%
Osteopenia	15%	33%	40%	35%
Osteoporosis	1%	1%	13%	27%
Established osteoporosis	1%	1%	7%	27%



Age	Average Woman		Average Man	
	mg/cm ²	T-score	mg/cm ²	T-score
25	955	zero	1055	+0.81
35	945	-0.08	1038	+0.67
45	920	-0.28	1002	+0.38
55	876	-0.64	990	+0.28
65	809	-1.19	969	+0.11
75	740	-1.75	928	-0.21
85	679	-2.24	859	-0.78

Risk Factor – Female Gender

The greater frequency of osteoporotic fractures in women has many causes:

- Women have lower peak bone mass – at age 35, men have 30 percent more bone mass than women, and they lose bone more slowly as they age
- Women generally have lighter, thinner bones than men to begin with so loss is more significant– also, the smaller periosteal diameter of bones in women also increases skeletal fragility
- The rapid decline in estrogen at menopause is associated with an increase in bone resorption without a corresponding increase in bone formation. This imbalance leads to an accelerated net loss of bone that results in decreased bone strength and ultimately may lead to fractures and osteoporosis. function at menopause (typically after age 50) precipitates such rapid bone loss such that most women meet the criteria for osteoporosis by age 70.
(For ex. Estrogen inhibits IL-2; IL-2 promotes osteoclast activity and therefore, bone resorption)
- Women may also lose bone during the reproductive years, particularly with prolonged lactation.
- Another reason for female predominance is that women live longer than men.

Other Risk Factors

Race. Caucasian and Asian women have lower bone density than blacks by as much as 5 to 10 percent. Until recently it was thought that Caucasian women were at greatest risk for osteoporosis, but a recent large-scale study has found that Hispanic, Asian, and Native American women are at least as likely to have low bone mass as Caucasians. And one-third of African American women are also at risk.

Build. Having a delicate frame or weaker bones predisposes you to a higher fracture risk. Overall muscle tone also plays a role in the likelihood of sustaining an injury.

Other Risk Factors

Onset of Menopause. Undergoing early menopause, naturally or surgically, increases your risk, because you will have reduced levels of estrogen for a longer period of time than you would with normal menopause. Because of the abrupt cessation of estrogen production that accompanies surgical menopause, women whose ovaries are removed (69 percent in one study) tend to show signs of osteoporosis within 2 years after surgery if no hormone replacement therapy is instituted. When medically possible, doctors recommend keeping your ovaries intact in order to maintain estrogen production, even if a hysterectomy (removal of the uterus) is necessary.

Heredity. Having a mother, grandmother, or sister with a diagnosis of osteoporosis or its symptoms ("dowager's hump" or multiple fractures) increases your risk. Body type, as well as a possible genetic predisposition to osteoporosis, can be passed from one generation to the next.

Classification of Osteoporosis

Primary osteoporosis in the elderly can be classified as type I or II:

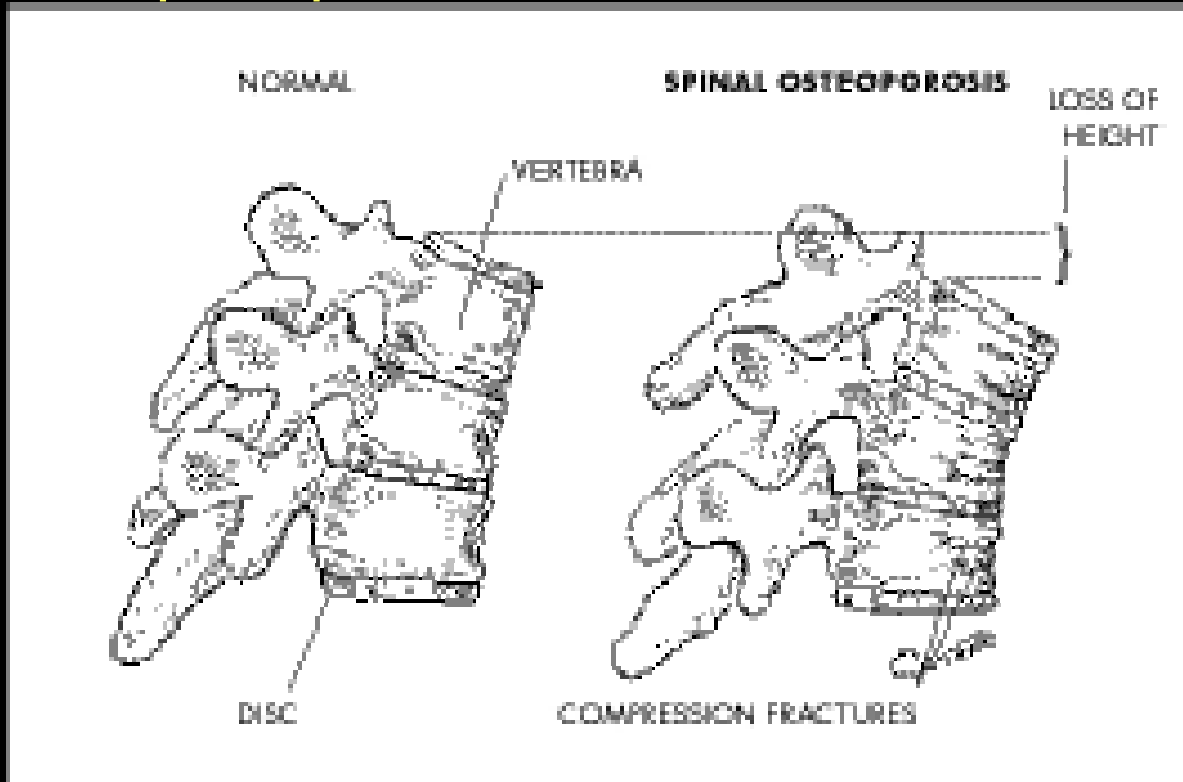
- **Type I** (menopausal) osteoporosis occurs mainly in persons aged 51 to 75, is six times more common in women, and is associated with vertebral and Colles' (distal radius) fractures.
- **Type II** (senescent) osteoporosis occurs in persons > 60, is two times more common in women, and is associated with vertebral and hip fractures.
- **Overlap between types I and II is substantial, so this classification is of limited clinical use.**

Primary osteoporosis is thought to result from the hormonal changes that occur with age, particularly decreasing levels of sex hormones (estrogen in women, testosterone in men). Several other risk factors are usually contributory.

Secondary osteoporosis may be due to many causes. (See risk factors page for conditions) Distinguishing secondary osteoporosis is important in patients of all ages, **because many of the causes are treatable** or have an important effect on prognosis

Osteoporosis – Vertebral Fractures

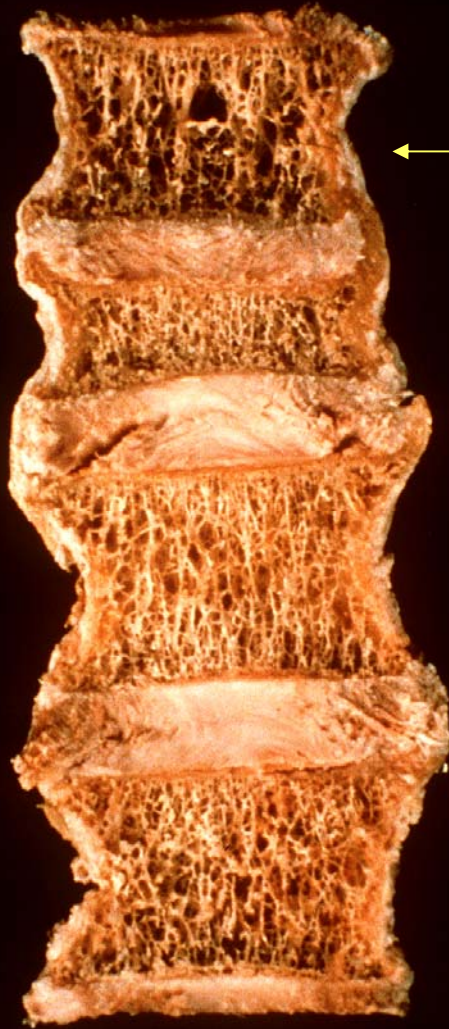
- A loss of height may indicate a vertebral compression fracture, which occurs in many patients without trauma or other acute precipitant.



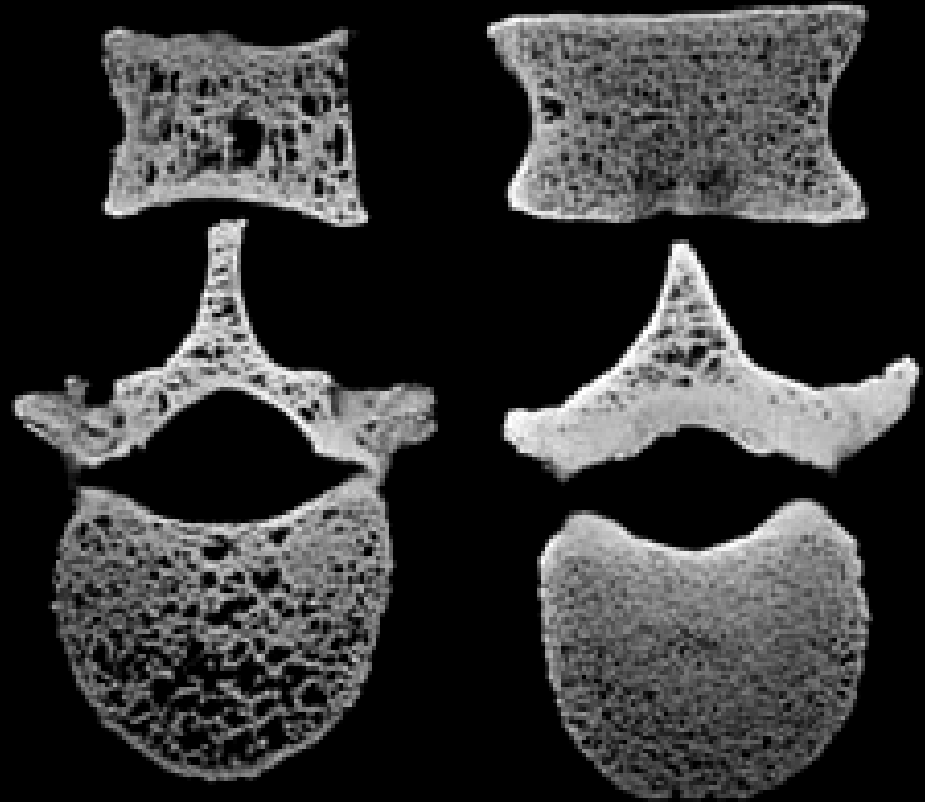
A persistent low backache, or sudden localized pain, could be a warning sign of compression fractures in the vertebrae of the spine.

But for many, these breaks cause little pain, and may go undetected for years. For some, the only tip-off is a noticeable loss of height, which can reach as much as 8 inches.

Osteoporosis – Vertebral Body Changes



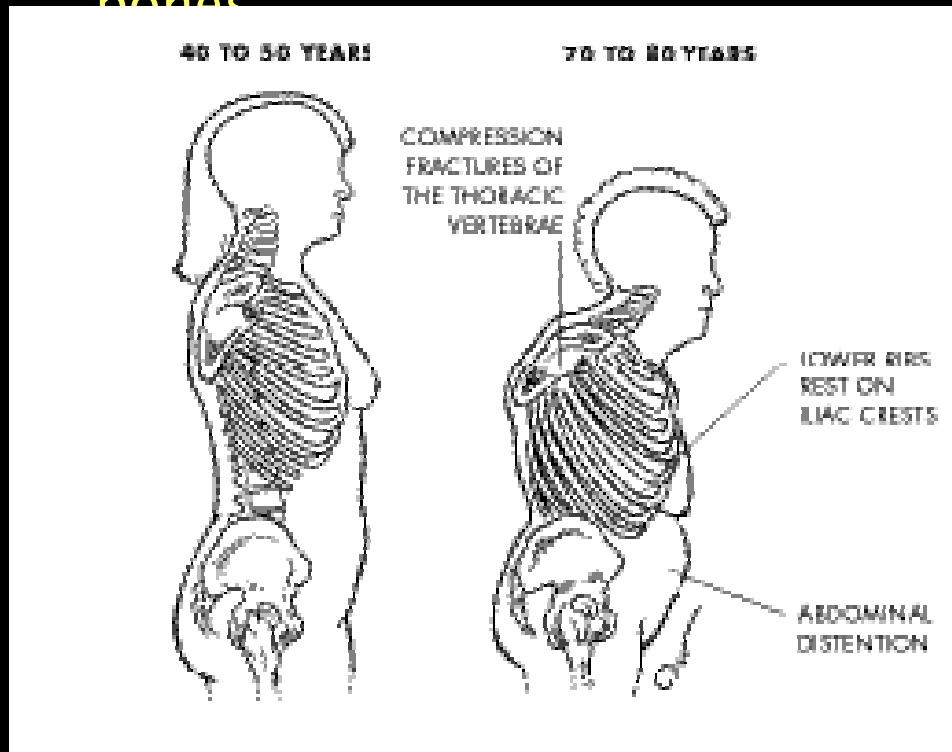
Osteoporosis – compression fracture.
Trabecular architecture is classic



Normal vertebral bodies on right

Osteoporosis – Dorsal Hyphosis

Dorsal kyphosis with exaggerated lordosis (dowager's hump) may result from multiple compression fractures. The hump caused by spine fractures is disfiguring. This is the feature of osteoporosis that is the worst thing for most patients. In severe cases, the ribs can touch the pelvic bones.

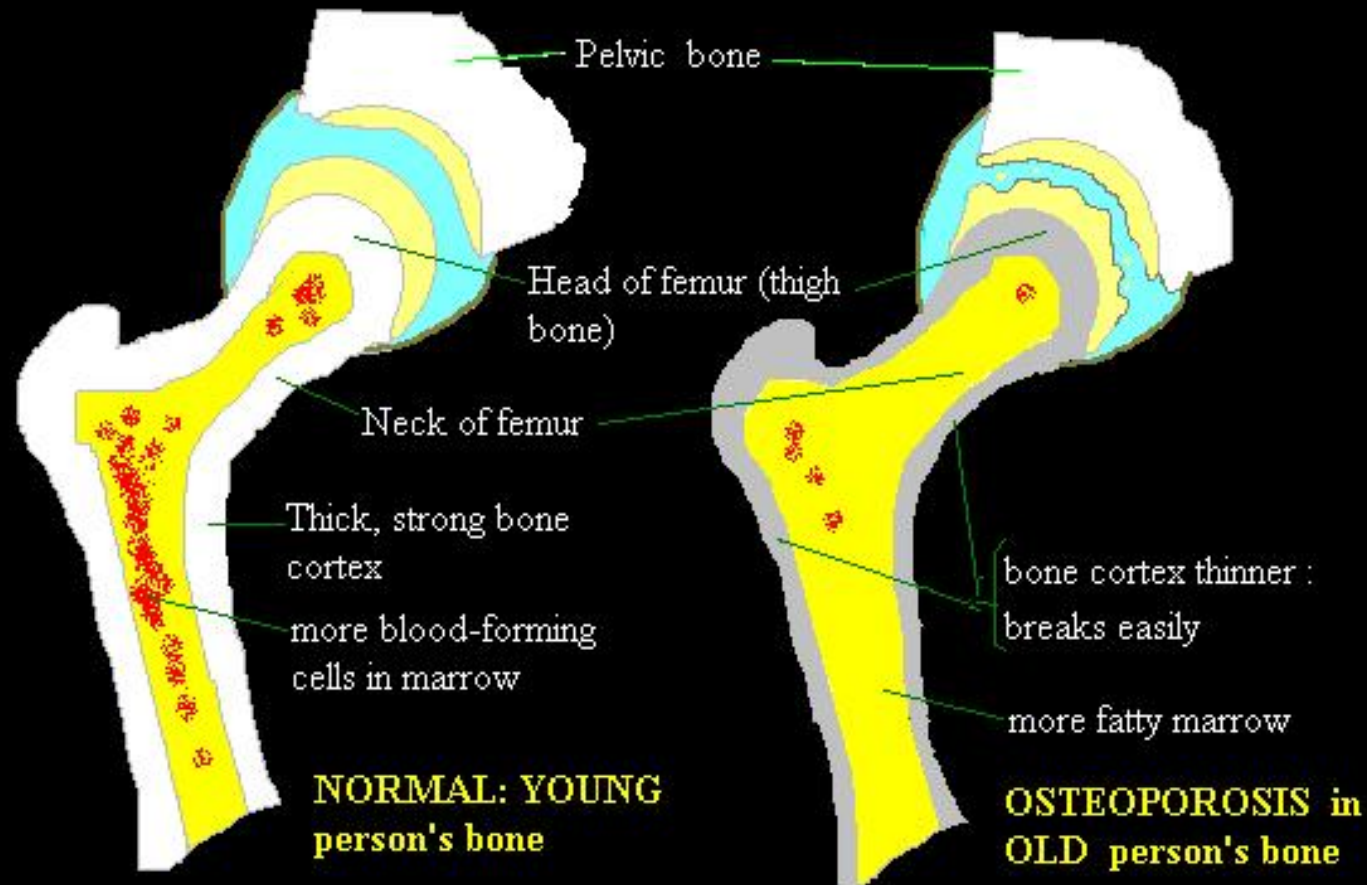


Along with the curve in the spine comes an outward curve of the stomach. Women do not realize that the curvature of the spine means the intestines have nowhere to go except forwards.

Many women think that they are getting fat, and they go on a diet trying to regain their youthful waistline. If they do successfully lose weight, it will only increase their risk for more osteoporotic fractures.

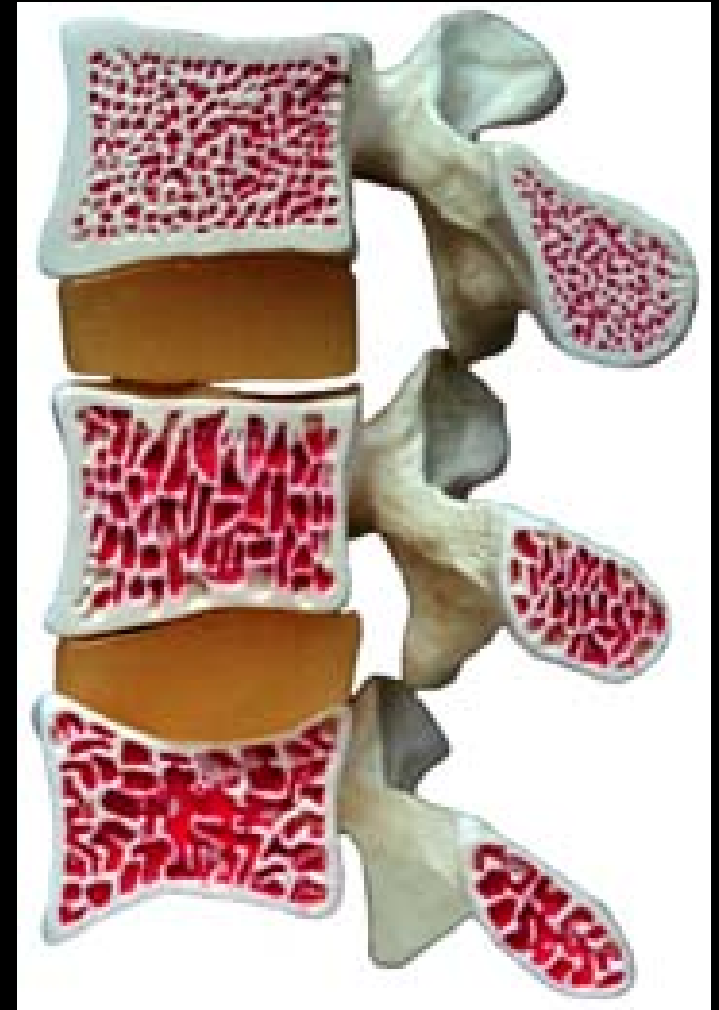
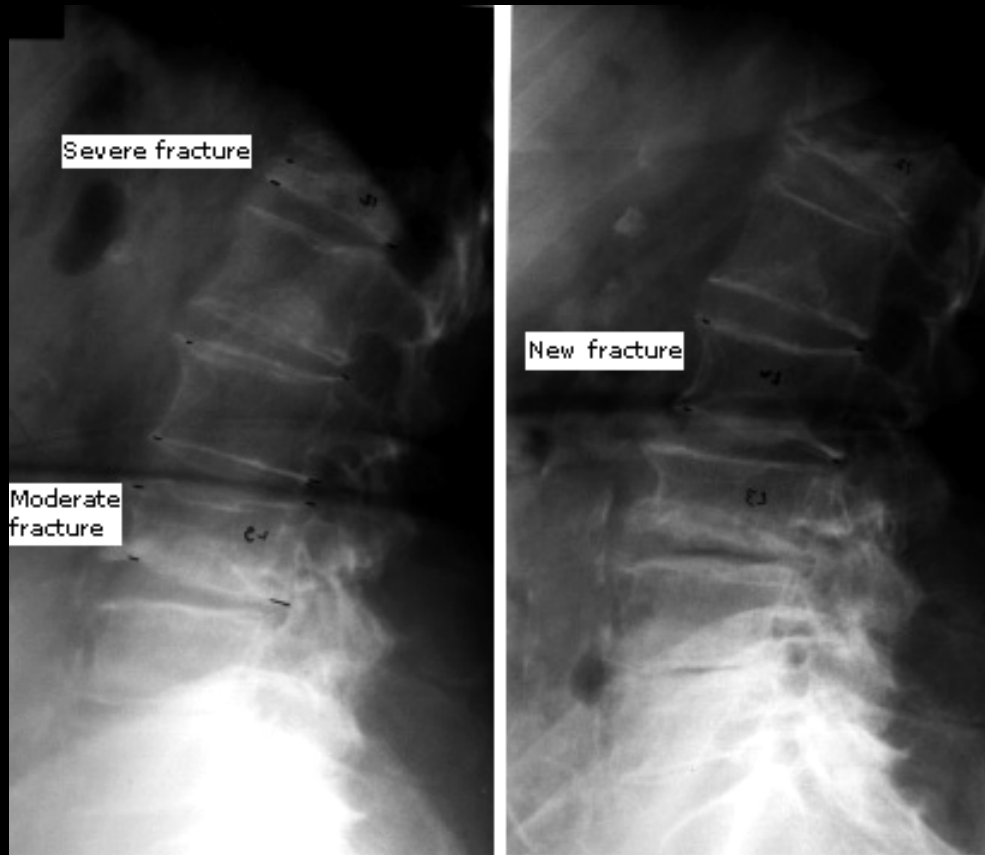
Osteoporosis – Other Fractures

- Osteoporotic fractures commonly affect the hip because the elderly tend to fall sideways or backwards, landing on this joint. Younger, more agile persons tend to fall forward, landing on the outstretched wrist, thus fracturing the distal radius



Upper third of THIGH BONE (Femur)

Radiographic Fracture Assessment



Patient who had a severe fracture and a moderate fracture in her spine. Three years later a second xray revealed a new fracture. These fractures were in the lower spine.

Osteoporosis – Diagnosis

Without a fracture or bone density screening there is no way to diagnose the presence of osteoarthritis.

The goal is to get as much information about compounding risk factors:

- A complete history of menstrual function, pregnancy, and lactation should be obtained in women, and a history of sexual function should be obtained in men, in whom decreased libido and erectile dysfunction may be due to low testosterone levels.
- Neurologic deficits and drugs that might increase the risk of falls should be analyzed.
- The family history should include fractures and evidence of endocrinopathy or renal calculi.
- One of the most important predictors of osteoporotic fractures is a history of a fracture after age 40 due to minimal or moderate trauma. In such persons, the fracture risk may be increased severalfold.
- The physical examination is often unremarkable. Spinal deformity and tenderness over the lower back should be sought.

Osteoporosis – Screening

X-ray findings are generally insufficient for the screening of primary osteoporosis:

- A normal x-ray of bone cannot reliably measure bone density but is useful to identify spinal fractures, explains back pain, height loss or kyphosis.
- X-rays may detect osteopenia only when bone loss is $> 30\%$.
- X-ray findings can also suggest other causes of metabolic bone disease, such as the lytic lesions in multiple myeloma and the pseudofractures characteristic of osteomalacia.

Bone densitometry is the only method for diagnosing or confirming osteoporosis in the absence of a fracture

- The National Osteoporosis Foundation recommends that bone densitometry be performed routinely in all women > 65 , particularly in those who have one or more risk factors.
- Densitometry can also be used for monitoring the response to therapy.

Screening – DEXA

Dual energy x-ray absorptiometry (DEXA)

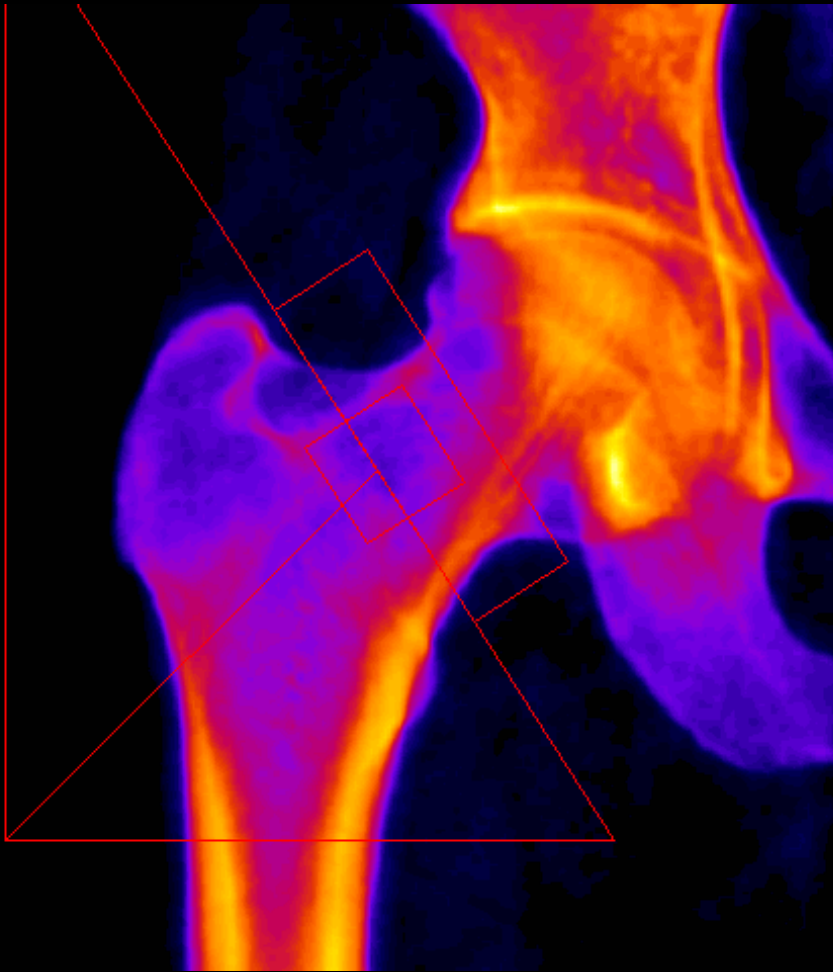
- DEXA measures areal density (ie, g/cm²) rather than true volumetric density.
- The test is non-invasive and involves no special preparation.
- Radiation exposure is minimal, and the procedure is rapid. This is the most popular and accurate test to date and the test only takes about 20 to 40 minutes, with a 5 mrem dose of radiation (a full dental x-ray is 300 mrem).

Screening – DEXA

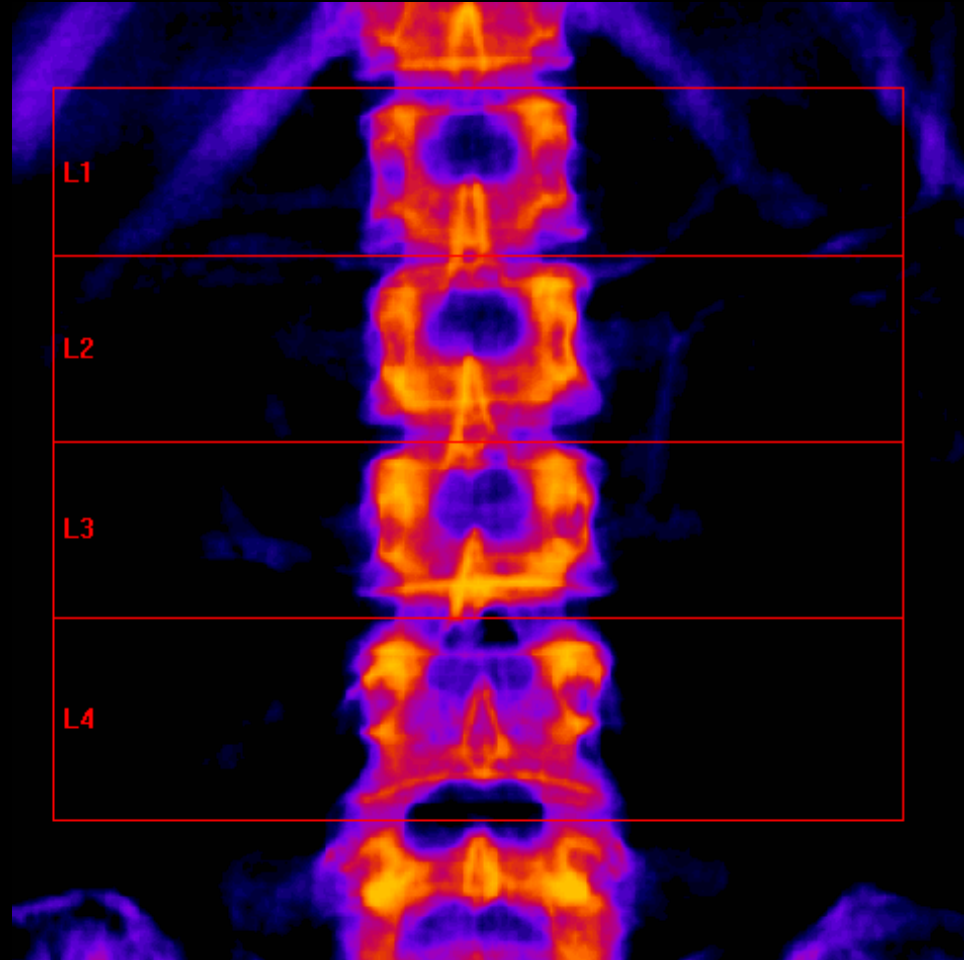


- Can be used to measure bone mineral density in the spine, hip, wrist, or total body.
- However, the standard apparatus is expensive and not portable. Small DEXA machines that can measure the forearm, finger, or heel are less expensive and are portable.

Screening – DEXA



DEXA of the proximal femur in a young woman, age 37, with unsuspected femoral-neck osteopenia (T score, -1.6).



DEXA of the lumbar spine in a young woman, age 37, with unsuspected lumbar spine osteopenia (T = -1.8).

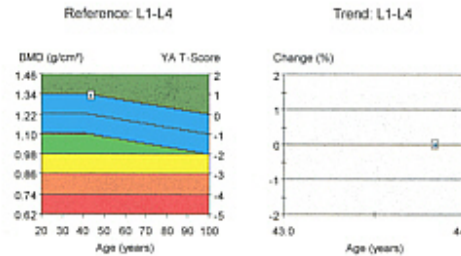
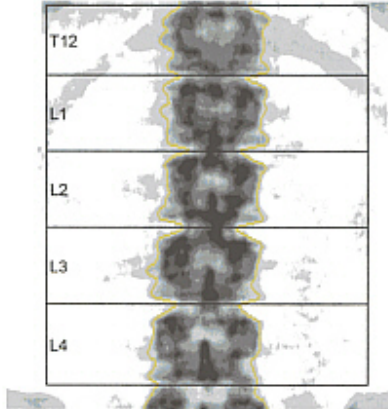
Screening – DEXA

University Medical Associates

1303 D'Antignac Street
Augusta, GA 30901

Facility ID: Measured: 09/16/1999 1:53:54 PM (2.05)
 Birth Date: 43.8 (years) Analyzed: 09/16/1999 1:56:30 PM (2.05)
 70.0 in. 175.0 lbs. White Male Printed: 04/27/2001 2:42:04 PM (2.15)
 Physician:

AP SPINE BONE DENSITY



Region	BMD ¹ (g/cm ³)	Young-Adult ² T-Score	Age-Matched ³ Z-Score
L1	1.345	1.5	1.5
L2	1.391	1.3	1.3
L3	1.378	1.1	1.2
L4	1.236	0.0	0.0
L1-L4	1.334	0.9	1.0

Region	Measured Date	BMD ¹ (g/cm ³)	Change (%)	Age (years)
L1-L4	09/16/1999	1.334	0.0	43.8

COMMENTS:

Image not for diagnosis
 76:3.00:50.00:12.0 0.00:9.38 0.00x1.05 20.7.%Farr:36.2%
 0.00:0.00 0.00 0.00

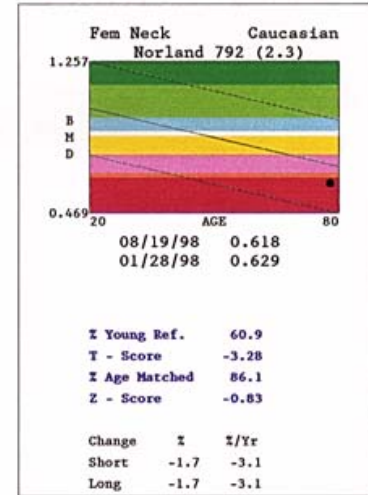
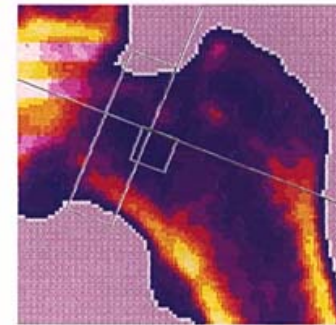
1 - Statistically 68% of repeat scans fall within 1SD (± 0.010 g/cm³ for L1-L4)
 2 - USA, AP Spine Reference Population, Ages 20-40
 3 - Matched for Age, Weight (males 25-100 Kg), Ethnic
 11 - WHO has defined for white women that >-1.0 SD = normal; -1.0 to -2.5 SD = osteopenia; <-2.5 SD = osteoporosis

SCOTT AND WHITE CLINICAL STUDIES UNIT TEMPLE TEXAS

Name ID Ethnic Caucasian
 Age 78 Sex Male Height 65
 Weight 167

L H

Left Hip on



Bone image not for diagnosis

	BMD g/cm ²	BMC g	LENGTH cm
Fem Neck	0.618	3.187	1.30
Troch	0.605	8.023	
Wards Tri	0.347	0.347	1.00

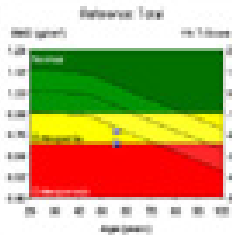
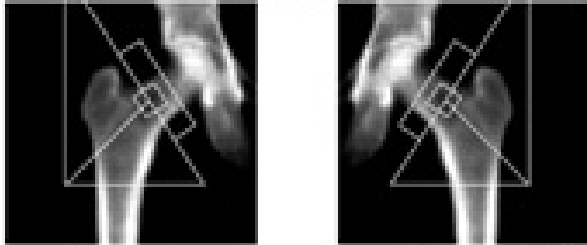
STD CVs for Neck BMD: 1.2 BMC: 1.7 See Guide for other CVs.
 1.0 x 1.0 mm, 90 mm/s, 9.00 cm Rev. 3.1.3/2.0.0 Calib. 08/19/98

COMMENTS

Screening – DEXA

Report	108 (4)	Facility ID:	
Exam Date:	09/16/1999 00:00:00	Physician:	
Height (cm/feet):	68.0 in. 5'8.0 in.	Measured:	09/16/1999 2:09:55 PM
Sex / Ethnic:	Female / White	Analysed:	09/16/1999 2:09:55 PM

Dual Femoral Density



Region	BMD ¹ (g/cm ³)	Young-Adult ² Z-Score	Age-Matched ³ Z-Score
Total	0.978	-0.9	-0.9
Left	0.958	-0.9	-1.0
Right	0.998	-0.8	-0.8
Difference	0.040	-	-

Comments:

Image not for diagnosis
 78.3 00.50 00:12.0 00:11.70 0.60x1.05 14.9 %Fat=20.6%
 0.00 0.00 0.00 0.00
 Neck Angle (deg) = 54
 (Please refer to report for details)
 Reference: 108 (4) 10/16/1999

1 - Statistically 68% of repeat scans fall within 1SD (± 0.020 g/cm³ for Total)
 2 - USA, Femur Reference Population, Ages 20-40
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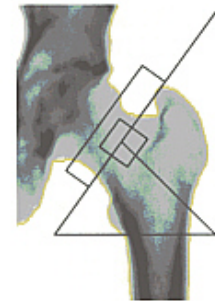
University Medical Associates

1303 D'Antignac Street
 Augusta, GA 30901

DUALFEMUR BONE DENSITY

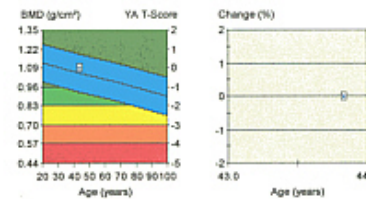
Facility ID:
 Birth Date: 43.8 (years)
 70.0 in. 175.0 lbs. White Male
 Physician:

Measured: 09/16/1999 1:57:13 PM (2.05)
 Analyzed: 09/16/1999 1:57:50 PM (2.05)
 Printed: 04/27/2001 2:41:26 PM (2.15)



Reference: Total

Trend: Total



Region	BMD ¹ (g/cm ³)	Young-Adult ² T-Score	Age-Matched ³ Z-Score
Neck	0.909	-1.2	-0.9
Wards	0.836	-1.0	-0.4
Troch	0.968	0.3	0.5
Shaft	1.286	-	-
Total	1.058	0.0	0.3

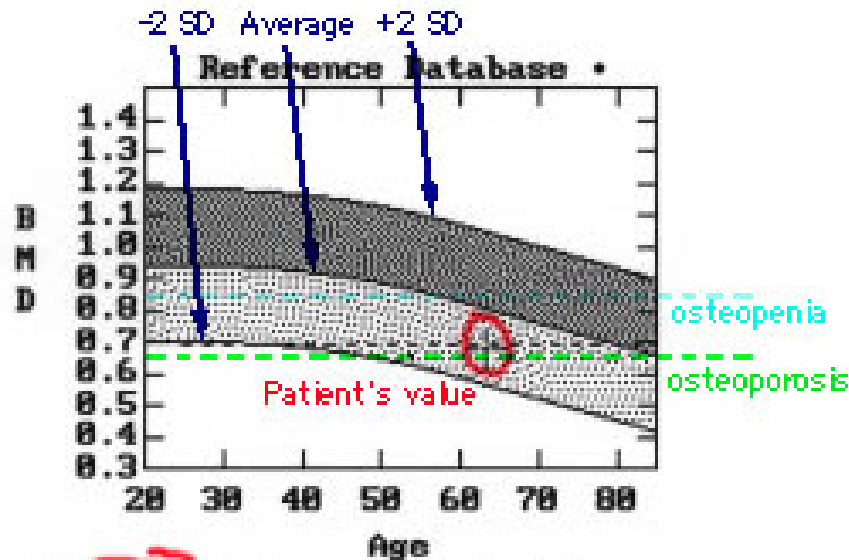
Region	Measured Date	BMD ¹ (g/cm ³)	Change (%)	Age (years)
Total	09/16/1999	1.088	0.0	43.8

COMMENTS:

Image not for diagnosis
 78.3 00.50 00:12.0 00:11.70 0.60x1.05 14.9 %Fat=20.6%
 0.00 0.00 0.00 0.00
 Neck Angle (deg) = 54

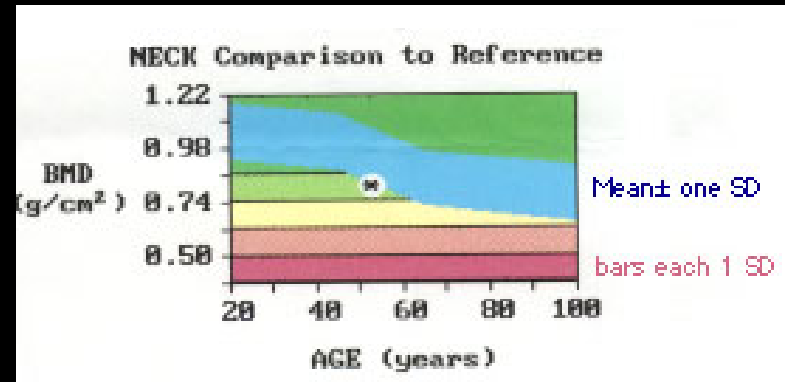
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 11 - WHO has defined for white women that >-1.0 SD = normal; -1.0 to -2.5 SD = osteopenia; <-2.5 SD = osteoporosis

Screening – DEXA



BMD(Total[L]) = 0.678 g/cm²

Check which region of interest is being plotted



REGION	BMD ¹ g/cm ²	Young Adult ² %	T	Age Matched ³ %	Z
L1	1.073	95	-0.48	97	-0.27
L2	1.097	91	-0.85	93	-0.65
L3	1.043	87	-1.30	89	-1.10
L4	1.129	94	-0.59	96	-0.39
L1-L2	1.087	94	-0.53	97	-0.32
L1-L3	1.071	92	-0.83	93	-0.62
L1-L4	1.087	92	-0.77	94	-0.57
L2-L3	1.070	89	-1.08	91	-0.88
L2-L4	1.091	91	-0.91	93	-0.71
L3-L4	1.088	91	-0.94	93	-0.73

Screening– Ultrasound Densitometry

Ultrasound densitometry can assess the density and structure of the skeleton and appears to predict fracture risk in the elderly. The apparatus is relatively inexpensive, portable, and uses no radiation but can be used only in peripheral sites (eg, the heel), where bone is relatively superficial. Ultrasound devices measure the speed of sound (SOS), as well as specific changes in sound waves (broadband attenuation or BUA) as they pass through bone. QUS measurements provide information on fracture risk by providing an indication of bone density and possibly also information on the quality of the bone. Ultrasound devices do not expose the patient to ionizing radiation.



Osteoporosis – Treatment & Prevention

- Treatment of the patient with osteoporosis frequently involves management of acute fractures as well as treatment of the underlying disease
- Patients should be thoroughly educated to reduce the likelihood of any risk factors associated with bone loss and falling
- A large body of data indicates that optimal calcium intake reduces bone loss and suppresses bone turnover
- Routine to recommend supplemental vitamin D
- Exercise in young individuals increases the likelihood that they will attain the maximal genetically determined peak bone mass. Meta-analyses of studies performed in postmenopausal women indicate that weight-bearing exercise prevents bone loss but does not appear to result in substantial bone gain
- Osteoporosis does not directly cause death. However, an excess mortality of 10 to 20% occurs in patients with established osteoporosis, particularly those with hip fractures.
- Prevention of osteoporotic fractures is critical to avoid a worldwide, costly epidemic. Prevention programs should be developed for patients at risk and for patients with diagnosed osteoporosis.

Osteoporosis – Treatment & Prevention

- **Antiresorptive therapy:** Persons with low bone mass and multiple risk factors, particularly those who have already had an osteoporotic fracture, should be considered for antiresorptive therapy. Antiresorptive drugs include estrogens, bisphosphonates, selective estrogen receptor modulators, and calcitonin.
- **Estrogen can prevent menopausal bone loss in most women.** Estrogen replacement therapy (ERT) is the treatment of choice for postmenopausal women, particularly those who had an early menopause, and for women who have had a hysterectomy. ERT is particularly effective during the first few years after menopause when bone loss is most rapid. Epidemiologic studies and the few prospective clinical trials of estrogen suggest that ERT or HRT decreases the risk of osteoporotic fractures by 30 to 50%. Because other antiresorptive drugs may have an additive effect when given with estrogen, combination therapy should be considered in patients who have very low bone density, continue to lose bone, or incur a fracture while taking ERT or HRT.

Osteoporosis – Treatment & Prevention

- **Bisphosphonates** are potent antiresorptive drugs that directly inhibit osteoclast activity. For women who cannot tolerate estrogen or have contraindications (eg, preexisting breast cancer, risk factors for breast cancer), bisphosphonates are considered the next choice; these drugs increase bone mass and decrease the risk of fractures, particularly in patients taking glucocorticoids. Bisphosphonates, particularly alendronate, have also decreased the incidence of vertebral and nonvertebral fractures by $\geq 50\%$ in large cohorts of postmenopausal women.
- Alendronate is used to prevent (5 mg/day) and treat (10 mg/day) osteoporosis. Pamidronate is available IV for treatment of hypercalcemia of malignancy and Paget's disease but has been used in osteoporosis.

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- Selective estrogen receptor modulators (SERMs) have been developed that are antiestrogenic and have antiresorptive effects on bone.
- Calcitonin has been used for many years in the prevention and treatment of osteoporosis.
- Other therapies: Anabolic therapies are under study; none is approved for osteoporosis. Intermittent injections of parathyroid hormone and fluoride stimulate bone formation and inhibit bone resorption, but their safety and efficacy remain to be established. Thiazides can decrease urinary calcium excretion and slow bone loss. They may be particularly useful in patients with hypercalciuria and osteoporosis (eg, those with idiopathic hypercalciuria).

...The End